CONVERSION OF SOME MANNICH BASES AND THEIR QUATERNARY SALTS TO ALDEHYDES

BY

HOMER JENNINGS SIMS

M.S., Western Illinois State College, 1948

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
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R. UNIV. BIBLIOTHEEK LEIDEN

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Introduction

The formation of indole-3-aldehyde from hexamethylenetetramine and gramine, the Mannich base from indole, formaldehyde and dimethylamine, was first observed in this laboratory in 1949.[1] Since such Mannich bases are easily prepared, the new reaction appears attractive as a method of synthesis of aldehydes. The present work was undertaken to determine whether, by changes in the reaction conditions, the yield of indole-3-aldehyde could be increased to a figure of preparative interest, and whether the reaction could be applied to the conversion of other Mannich bases to aldehydes.

Discussion of Results

A study of the reaction conditions for the synthesis of indole-3-aldehyde by the reaction of gramine (3-dimethylaminomethylindole) with hexamethylenetetramine in the presence of an organic acid has been made. Under the optimum conditions found the pure aldehyde is produced in 53 per cent yield.

Mannich bases, other than gramine, related to indole also yield indole-3-aldehyde. Diethylaminomethylindole and piperidinomethylindole were found to provide the aldehyde in yields of 48 per cent and 40 per cent respectively. Similarly, Mannich bases from substituted indoles may be converted to the substituted 3-indolealdehydes by this method. The conversion of 2-phenyl-3-dimethylaminomethylindole to 2-phenylindole-3-aldehyde was accomplished in 70 per cent yield. When the 2-substituent was a methyl group, the yield of aldehyde, isolated as the phenylhydrazone, was very poor.

The piperidine Mannich base of *beta*-naphthol can be converted to the aldehyde only in poor yield (20 per cent) by the

new reaction and other phenolic Mannich bases which have been studied give even poorer yields of aldehydes. No product at all was obtained from 1-morpholinomethyl-2-naphthol. The formation of a phenol-formaldehyde type resin was the only apparent reaction in the case of the Mannich base from *o*-cresol. No successful application of the reaction to a ketonic Mannich base has been found. The failure to convert *beta*-dimethylaminopropiophenone and 2-dimethylaminomethyl-cyclohexanone to the aldehydes is apparently due to the ease with which the olefin is formed by splitting out dimethylamine. The Mannich bases from phenylacetylene and from 2-nitro-propane were used in this reaction without success. Thus, the synthesis of aldehydes by this route appears limited to indole and its derivatives, in which field, however, it is the method of choice.

It is probable that the reaction of gramine with hexamethylenetetramine in acid solution proceeds by amine exchange, yielding the 3-indolemethylhexamethylenetetrammonium ion which decomposes to the aldehyde as in the Sommelet synthesis.[2,3] Support for this view is found in the fact that benzyldimethylphenylammonium chloride reacts with hexamethylenetetramine in chloroform to give the expected quaternary salt, benzylhexamethylenetetrammonium chloride.

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VITA

The author was born in La Prairie, Illinois, on August 26, 1925. He attended the public schools there and graduated from La Prairie Community High School in 1942. He received a state scholarship and entered Western Illinois State College at Macomb, Illinois, in the fall of 1942. He was a member of the armed services from June 1944 to July 1946, when he returned to Western Illinois State College. He was awarded the degrees of Bachelor of Science and Master of Science in 1948. He entered the Graduate College of the University of Illinois as a teaching assistant in September 1948.